DOCKET NO.: ISIS-4943 Application No.: 09/996,263

Office Action Dated: August 12, 2003

## Amendments to the Specification

On page 6, please amend the first full paragraph (lines 11-19) as follows:

In accordance with this invention at least one of the 2'-deoxyribofuranosyl moiety of at least one of the nucleosides of an oligonucleotide is modified. A halo, alkoxy, aminoalkoxy, alkyl, azido, or amino group may be added. For example, F, CN, CF<sub>3</sub>, OCF<sub>3</sub>, OCN, O-alkyl, S-alkyl, SMe, SO<sub>2</sub>Me, ONO<sub>2</sub>, NO<sub>2</sub>, NH<sub>3</sub>, N<sub>3</sub>, NH<sub>2</sub>, NH-alkyl, OCH<sub>2</sub>CH=CH<sub>2</sub>, (allyloxy), OCH<sub>3</sub>=CH<sub>2</sub>, OCCH, where alkyl is a straight or branched chain of  $C_1$  to  $C_{20}$ , with unsaturation within the carbon chain.

Please amend the paragraph beginning on page 10, line 27 to page 11, line 4, as follows:

It is desired that the oligonucleotides of the invention be adapted to be specifically hybridizable with the nucleotide sequence of the target RNA or DNA selected for modulation. Oligonucleotides particularly suited for the practice of one or more embodiments of the present invention comprise 2'-sugar modified oligonucleotides wherein one or more of the 2'-deoxy ribofuranosyl moieties of the nucleoside is modified with a halo, alkoxy, aminoalkoxy, alkyl, azido or amino group. For example, the substitutions which may occur include F, CN, CF<sub>3</sub>, OCF<sub>3</sub>, OCN, O-alkyl, S-alkyl, SMe, SO<sub>2</sub>Me, ONO<sub>2</sub>, NO<sub>2</sub>, NH<sub>3</sub>, NH<sub>2</sub>, NH-alkyl, OCH<sub>3</sub>=CH<sub>2</sub>, OCH=CH<sub>2</sub> and OCCH. In each of these, alkyl is a straight or branched chain of C<sub>1</sub> to C<sub>20</sub>, having unsaturation within the carbon chain. A preferred alkyl group is C<sub>1</sub>-C<sub>9</sub> alkyl.